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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,309	02/13/2002	Izumi Arai	P67183US0	7988

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,309	ARAI, IZUMI	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-13 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-13 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 13 February 2002 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pending claims are 1-13 as originally filed.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of copending Application No. 09/926,761. Although the conflicting claims are not identical, they are not patentably distinct from each other because present claims to methods of maintaining the health of a subject, method of reconstructing a body, methods of treating a subject by cloning are all encompassed by claims 1-5 of '761.

Present claims 1-13 are to methods of maintaining the health of a subject, method of reconstructing a body and methods of treating a subject by replacing an organ with a cloned organ. Claims 1-5 of '761 are drawn to methods of preventing or inhibiting aging of an individual comprising cloning a body, an organ, a tissue or a cell of the individual and replacing the body, organ, tissue or cell of the individual with the cloned body, organ, tissue or cell and a method of resurrecting an ancient creature using parthenogenesis. Both the present claims and those of '761 require or could require the cloning of a subject or individual and the transplantation of organs from the clone into the subject or individual. Thus at the time of the present invention, it would have been obvious to the ordinary artisan to arrive at the present invention given claims 1-5 of '761.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility.

> "Credible Utility" - An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. (see Utility Guidelines, www.uspto.gov)

Claim 8 is drawn to a method of treating a subject by replacing an organ in the subject with a cloned organ, wherein the method "diversly evolves the subject." This is a method of evolution. Given the immense time frame science has given for evolution and that the particular feature develops gradually over the time frame, the ordinary artisan would not believe that applicant's method could cause evolutionary diversity of any species.

Claim 8 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1-13 are rejected less than 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to methods of maintaining the health of a subject comprising the replacement of at least one organ with a cloned organ, a method of reconstructing the body from a cell of a subject comprising cloning the body from a cell, tissue or organ of the subject and methods of treating a subject comprising replacing at least one organ in the subject with at least one cloned organ, and repeating when the cloned organ becomes diseased.

The claims are not enabled because at the time of filing the, art taught that it was unpredictable to clone successfully for the breath of the claims which encompasses all mammals, reptiles, fish, birds and amphibians. Even for mammals, the art taught that their cloning was unpredictable. In regard to this, Westhusin, states that one of the major factors influencing a successful cloning outcome is species of target animal. Westhusin goes on to state that while the basic methodology for nuclear transfer may be similar, the specific materials and methods do not automatically apply across all species. Westhusin outlines six factors which contribute to successful cloning: 1) acquisition of mature ova, 2) removing the chromosomes contained within the ova, 3) transfer of cell nuclei obtained from the animal to be cloned into enucleated ova, 4) activation of the newly formed embryo, 5) embryo culture in vitro, and 6) transfer of the cloned embryo into a surrogate mother. There is no guidance in the specification or the art on, for example, activation of enucleated Drosophila eggs or lobster eggs, much less how to enucleate them for successful nuclear transfer. Westhusin further states that each of these steps will vary slightly between species, but that, more importantly, the efficiency of each step varies among species, ultimately affecting the ease of which a particular animal can be cloned (Westhusin, page 36-37, bridg. parag.). This analysis is supported by Polejaeva that states, in regard to the inefficiency of cloning, that several factors affect the inefficiency: laboratory to laboratory variation, oocyte source and quality, methods of embryo culture, donor cell type, possible loss of somatic imprinting in the nuclei of the reconstructed embryo, failure to reprogram the transplanted nucleus adequately, and failure of artificial methods of

activation to emulate reproducibly those crucial membrane-mediated events that accompany fertilization (Polejaeva, page 1, parag. 2). Thus nuclear transfer, at the time of filing was not routine, but requires extensive experimentation without a predictable degree of success. Pennisi and several scientists working in the area of mammalian cloning point to a lack of general and reproducible success emphasize this. Robert Wall of the USDA is quoted as stating that despite years of effort, "[w]e're in the same bind that we've always been in. A majority of [would be clones] do not make it to term." (Pennisi, page 1722, col. 1, parag. 2, lines 9-14). Pennisi and Vogel state, "even when an embryo does successfully implant in the womb, pregnancies often end in miscarriages" (Pennisi, page 1722, col. 1, parag. 3, lines 16-18). Attempts to clone pigs using techniques successful in sheep were not successful; indicating that cross-species application of methodology is unpredictable (Pennisi, page 1725, col. 1-2, bridg. parag.). The case with rabbits indicates that obtaining an embryo by nuclear transfer does not translate into a cloned rabbit. While many cloned rabbit embryos can be made, they abort upon transfer to surrogate mothers, and in 2000, there had not been any successes in cloning rabbits (Pennisi, page 1725, col. 2, parag. 3). With primates, two cloned monkeys were produced, but there have been no subsequent successes in primate cloning (Pennisi, page 1726, col. 2, line 6 to col. 3, line 3). With regard to cats, one cloned cat has been produced, but given the difficulty in the art to produce a cloned cat and the lack of producibility as stated above, the cloning of cats is unpredictable. Two attempts to implant cat eggs or reconstructed embryos failed, providing for an unpredictable outcome for cat cloning (Pennisi, page 1726, col. 2, parag. 3, lines 4-5). Others have reported establishing pregnancies but no report of a cloned cat being born (Pennisi, page 1726, col. 2, parag. 3, lines 5-9 and 11-12). As the authors state, establishing pregnancies is only part of the problem and is not a guarantee of a cloned mammal being produced (Pennisi, page 1726, col. 2, lines 9-11). Thus, at the time of filing, there appears to be such unpredictability that only the cloning of sheep, cows, and rodents were predictable. Particularly noteworthy, given that applicant's claims encompass the cloning of humans, is a report that the cloning of monkeys, a primate, by nuclear transfer had been successful when embryonic cells were the nuclear donor, not when somatic cells

were used as nuclear donor (Mitalipov, abstract). Mitalipov further states, clearly, that somatic cell cloning, as is part of the present methods, has not been accomplished in primates (Mitalipov, page 1367, col. 2, parag, 3, lines 1-3). Simerly, states that in rhesus monkey NT units, DNA and microtubule imaging showed disarrayed mitotic spindles with misaligned chromosomes, which resulted in unequal chromosome segregation and aneuploid embryos (Simerly, page 297, col. 2, parag. 1, lines 5-11). Thus, primate cloning is unpredictable for all the reasons cited above.

It was known at the time of filing, that cross-species nuclear transfer was unpredictable in both embryo and term development. Meirelles demonstrate that methods of nuclear transfer where the nuclear material of *Bos indicus* is inserted into the oocyte of *Bos taurus* produces calves comprising the nuclear material of *Bos indicus* and the mitochondria of *Bos taurus*. Meirelles *et al.* teach that previous attempts to use the *Bos* oocyte as hosts for nuclear transfer from unrelated species allowed development to the blastocyst stage, however conclude that incompatibility among the nuclear and mitochondrial genetic systems is responsible for the early arrest. Meirelles *et al.* also point to similar failures using *Mus caroli* and *Mus musculus* citing Dominko *et al.* discussed in length in the previous office action. Meirelles *et al.* conclude that in light of their results and the failures of the prior art, that nuclear transfer across subspecies barriers is possible. (see Meirelles, pp. 351-355). Applicant's claims encompass nuclear transfer (cloning) when the nucleus is of one species and the oocyte is of another species. This clearly lacks predictability given the teaches of Meirelles. Further, in the production of sheep goat chimeras, there were biases towards chimeras whose genotype and phenotype was most like that of the recipient, and that the successful production of chimeras resided in the neutralization of incompatibility between the chimeric embryo (Fehilly et al (1985), page 221, parag. 1). This is also an unpredictable feature of the claimed invention as an embryo of one species implanted into a surrogate mother of another species is unlikely to develop given the teaching of Fehilly. The specification does not provide guidance on producing cross-species embryo or animals, nor how to overcome the unpredictable nature of cross-species cloning.

Further, the claims are not enabled as the claims state that a body, an organ, a tissue and a cell is cloned. However, the art, as indicated above at the time of filing, taught how to clone by nuclear transfer bovines, sheep and goats, there is no guidance on cloning a body, an organ, a tissue or a cell as an entity separate from the individual. Neither the specification nor the art teaches such.

Claim 9 is to a method of evolution, which clearly is not enabled by the specification. Applicant has provided no guidance as to what other steps need to be involved to cause evolution through nuclear transfer. Similarly, there is no guidance or discussion as to what characteristics or variations are achieved though this method.

The specification is deficient in providing any guidance on overcoming these art recognized unpredictabilities. There is no discussion or working examples, which describe cloning methods that permit the cloning of the diverse individuals encompassed by the claims. Further, there is no guidance or working example for cross-species nuclear transfer, also encompassed by the claims.

Therefore, in view of the reasons presented above, the claimed invention is unpredictable because at the time of filing the skilled artisan would need to engage in an undue amount of experimentation without a predictable degree of success to implement the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3 and 5-7 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kimikawa et al (1997) Transplantation 64, pp. 709-716.

Kimikawa teaches bone marrow and kidney transplantation in cynomolgus monkeys where the donor and recipient monkey were each male (page 709, col. 2, parag. 2, line 1 and page 710, col.1, parag. 8). The methods are either anticipated by or obvious over Kimikawa because a cloned organ, tissue or cell is indistinguishable from that of an organ, tissue or cell isolated from a donor of the same species and sex. Thus, as the methods used cloned organs, these organs would be indistinguishable from those isolated from living or cadaver donors. Each limitation of claims 1, 3 and 5-7 refers to the cloning method and does not distinguish between the cloned and noncloned organs, tissues and cells. In other words, in a side-by-side comparison, there is no way to distinguish between the cloned organs stated in the claim and those of Kimikawa. Thus, Kimikawa clearly anticipates or makes obvious methods of claims 1, 3 and 5-7.

Claims 1, 2, 4 and 8-13 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Brendel et al (1998) Transplantation Proceedings 30, pp. 309-311.

Brendel teaches transplantation of human cadaver pancreatic islets, at least one organ, into a patient with type 1 diabetes (page 309, col. 1, parag. 3). Type 1 diabetes in the results of a diseased pancreas that does not produce sufficient insulin to regulate blood glucose levels. The method of Brendel is not distinguishable from that of claims 1, 2, 4 and 8-13 because there is no distinction between the donor pancreatic islets and cloned pancreatic islets. The transplanted islets of Brendel are inherently better quality than those of the recipient; the transplantation improves the function of the pancreas, and renovates the life permanently of the recipient. As the method of Brendel cannot be distinguished from that of the claims, Brendel would inherently cause diverse evolution. Artificial materials are used in the isolation of the pancreatic islets of Brendel. The new pancreatic cells would

inherently have a new energy system. Thus, Brendel clearly anticipates or makes obvious the methods of claims 1, 2, 4 and 8-13.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-The, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0408. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

June 18, 2004